Remarks

To expedite allowance of claim 21, the Applicant has rewritten claim 21 in independent form to include the subject matter of claims 18 and 20. Accordingly, no new matter is introduced by the virtue of the amendment and its entry is respectfully requested.

Applicant appreciates the Examiner's indication that claims 14, and 16-17 appear to be allowable. The Examiner also indicated that claim 21 would be allowable if written in an independent form with all the limitations of the claims it depends from. Applicant has re-written claim 21 to include the limitations of claims 18 and 20.

The Examiner maintained rejection of claims 1, 4, 13, 18-20 and 22-23 under 35 U.S.C. § 112, first paragraph, as lacking an adequate written description.

The Applicant respectfully disagrees for the following reasons.

Applicant submits herewith a Third Declaration of David E. Fisher under 37 C.F.R. 1.132 (Dr. Fisher Declaration 3).

The present application teaches a method for diagnosing melanoma that involves determining whether a malignant cell expresses microphthalmia (Mi or MiTF or MITF) (par. 3, Dr. Fisher Declaration 3) by contacting a biological sample containing malignant cells with a probe that recognizes microphthalmia (par. 2, Dr. Fisher Declaration 3). Accordingly, the Applicant discovered that melanoma can be diagnosed by detecting presence of a particular protein, Mi, in malignant cells (par. 3, Dr. Fisher Declaration 3). Thus, the claims are directed to a method for diagnosing melanoma by detecting Mi in the malignant cells.

The current claims are directed to an immunohistochemical approach that uses an antibody that will bind specifically to Mi. It is not necessary that that antibody distinguishes between the different isoforms of Mi, but merely that the antibody selectively binds to Mi (par. 4, Dr. Fisher Declaration 3).

The skilled artisan knows that an antibody that selectively binds to a protein means that the antibody would not cross-react with a wide range of proteins. In other words, it must have the ability to be able to sufficiently discriminate between multiple proteins to accomplish the desired result. (par. 5, Dr. Fisher Declaration 3). In the specification, the Applicant exemplifies

preparing an antibody that selectively binds to human Mi, namely, the monoclonal antibody D5. The Applicant points out that one can use the amino terminal Taq-Sac fragment of human Mi cDNA and use this to generate an antibody that will selectively bind to human Mi. (par. 6, Dr. Fisher Declaration 3).

The skilled artisan was well-aware of how to prepare antibodies. The sequence of human Mi was known. Indeed, a discussion of Mi and Mi mutants and analogues is set out at pages 5 and 6 of the specification. Methods for preparing such antibody are provided in the specification at pages 13 – 15. (par. 7, Dr. Fisher Declaration 3). Homologous regions with related proteins were also known (par. 8, Dr. Fisher Declaration 3).

It is known that one can generate antibodies using fragments that are as small as six amino acids. Methods for enhancing the ability of a particular fragment to generate an amino acid that will bind to that fragment are known. (par. 9, Dr. Fisher Declaration 3).

Consequently, it is clear that the skilled artisan, based on what the Applicant taught and demonstrated in view of the state of the art, knew what was being described by the reference to Mi antibodies. (par. 10, Dr. Fisher Declaration 3).

Moreover, it was well known at the time of filing that multiple methods could be used to prepare such an antibody. For example, using a phage display system, antibodies could be made completely in vitro, bypassing the immunization step. Such a method would rely only on screening to identify an antibody with the desired property, i.e., one that will selectively bind Mi. (par. 11, Dr. Fisher Declaration 3).

The skilled artisan also knows that antibodies, unlike many other types of proteins, and certainly nucleic acids, are typically **not defined by an amino acid sequence** or a nucleotide sequence, **but rather** by **their ability to bind a particular protein**. This is because of how well known and standard these procedures are in the art. (par. 12, Dr. Fisher Declaration 3).

The Examiner argued that because antibodies are screened and tested to ensure they have the desired activity, there is not a written description of such an antibody. The Applicant disagrees. Selection of a desired type and affinity of produced antibodies by screening is part of any method of making antibodies. For example, *Hoogenboom* shows a routine method of

making antibodies in Figure 1 at page 64. In this method, one first constructs a library and then enriches the antigen-specific antibodies using affinity selection. Since the early '80's, when people were producing monoclonal antibodies, the screening of hybridomas to select those that expressed an antibody with a desired characteristic was always considered a necessary and routine part of the manufacture of such an antibody. This is how the field looks at and describes antibodies. (par. 15, Dr. Fisher Declaration 3).

Accordingly, the present specification provides the type of guidance and description necessary here. The Applicant has also previously indicated, that it was not necessary for the antibody to distinguish between different isoforms of Mi. (par. 13, Dr. Fisher Declaration 3). It is not necessary for this antibody to bind to some specific binding site on the protein because one is **not looking to block some activity** as one might with certain therapeutics. Rather, the **goal is to identify whether or not Mi is present**. (par. 14, Dr. Fisher Declaration 3).

The Examiner argued that she sees no nexus between the present invention and Capon v. Eshhar, 418 F.3d 1349 (Fed. Cir. 2005). Applicant respectfully disagrees. The Court specifically held that the "written description" requirement does not require "that every invention must be described in the same way." 418 F.3d at 1358. The court explained:

> As each field evolves, the balance also evolves between what is known and what is added by each inventive contribution [418 F.3d at 1358]

As explained above, when one looks at what the invention that is being claimed is, and the antibody field, it is clear that the specification satisfies the written description requirement.

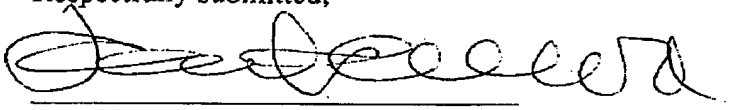
This is further confirmed by Dr. Fisher Declaration 3. The sequence of Mi was known (par. 7, Dr. Fisher Declaration 3), and homologous regions with related proteins were known, (par. 8, Dr. Fisher Declaration 3).

Accordingly, Applicant respectfully submits that he has provided, as of the filing date, a precise definition of the claimed invention so as to distinguish it from others and such that the skilled artisan knows what is being described.

Accordingly, in view of the foregoing, Applicant respectfully submits that all claims comply with 35 U.S.C. § 112, first paragraph.

Applicant respectfully submits that all claims are in condition for allowance. Early and favorable action is requested.

Respectfully submitted,



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